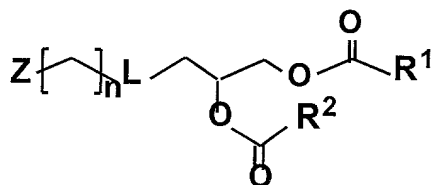


IT IS CLAIMED:

1. A composition for administration of a nucleic acid, comprising:

(a) liposomes comprised of

(i) a lipid having the formula



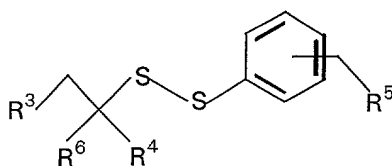
where each of R<sup>1</sup> and R<sup>2</sup> is an alkyl or alkenyl chain having between 8-24 carbon atoms;

n = 1-20;

L is selected from the group consisting of (1) -X-(C=O)-Y-CH<sub>2</sub>-, (2) -X-(C=O)-, and (3) -X-CH<sub>2</sub>-, where X and Y are independently selected from oxygen, NH and a direct bond;

Z is a weakly basic moiety that has a pK of less than 7.4 and greater than about 4.0; and

(ii) a compound having the general structure:



wherein R<sup>3</sup> is a hydrophilic polymer comprising a linkage for attachment to the dithiobenzyl moiety; R<sup>4</sup> is selected from the group consisting of H, alkyl and aryl; R<sup>5</sup> is selected from the group consisting of O(C=O)R<sup>7</sup>, S(C=O)R<sup>7</sup>, and O(C=S)R<sup>7</sup>; R<sup>7</sup> comprises an amine-containing lipid; and R<sup>6</sup> is selected from the group consisting of H, alkyl and aryl; and where orientation of CH<sub>2</sub>-R<sup>5</sup> is selected from the ortho position and the para position; and

(b) a nucleic acid associated with said liposomes.

2. The composition of claim 1, wherein X is NH and Y is oxygen.

3. The composition of claim 1, wherein L is a carbamate linkage, an ester linkage or a carbonate linkage.

4. The composition of claim 1, wherein L is  $\text{NH}-(\text{C}=\text{O})-\text{O}-\text{CH}_2$ .

5. The composition of claim 1, wherein Z is an imidazole.

6. The composition of claim 1, comprising between 1-80 mole percent of the lipid.

7. The composition of claim 1, wherein Z is a moiety having a pK value between 5.0-6.5.

8. The composition of claim 1, wherein each of  $\text{R}^1$  and  $\text{R}^2$  is an unbranched alkyl or alkenyl chain having between 8-24 carbon atoms.

9. The composition of claim 8, wherein each of  $\text{R}^1$  and  $\text{R}^2$  is  $\text{C}_{17}\text{H}_{35}$ .

10. The composition of claim 1, wherein n is between 1-10.

11. The composition of claim 1, wherein  $\text{R}^6$  is H and  $\text{R}^4$  is selected from the group consisting of  $\text{CH}_3$ ,  $\text{C}_2\text{H}_5$  and  $\text{C}_3\text{H}_8$ .

12. The composition of claim 1, wherein the amine-containing lipid comprises either a single hydrocarbon tail or a double hydrocarbon tail.

13. The composition of claim 1, wherein the amine-containing lipid is a phospholipid having a double hydrocarbon tail.

14. The composition of claim 1, wherein  $R^4$  and  $R^6$  are alkyls.

15. The composition of claim 1, wherein  $R^3$  is selected from the group consisting of polyvinylpyrrolidone, polyvinylmethylether, polymethyloxazoline, polyethyloxazoline, polyhydroxypropyloxazoline, polyhydroxypropyl-methacrylamide, polymethacrylamide, polydimethyl-acrylamide, polyhydroxypropylmethacrylate, polyhydroxyethylacrylate, hydroxymethylcellulose, hydroxyethylcellulose, polyethyleneglycol, polyaspartamide, copolymers thereof, and polyethyleneoxide-polypropylene oxide.

16. The composition of claim 1, wherein  $R^3$  is polyethyleneglycol.

17. The composition of claim 16, wherein  $R^6$  is H and  $R^4$  is  $CH_3$  or  $C_2H_5$ .

18. The composition of claim 1, wherein said liposomes include between 5-20 mole percent of the compound.

19. The composition of claim 1, further including a therapeutic compound entrapped in the liposomes.

20. The composition of claim 1, wherein said nucleic acid is entrapped in at least a portion of said liposomes.

21. The composition of claim 20, wherein the nucleic acid is selected from DNA, RNA, fragments thereof and oligonucleotides.

22. The composition of claim 1, further including a ligand for targeting the liposomes to a target site, said ligand covalently attached to a distal end of the hydrophilic polymer R<sup>3</sup> on said compound.

5

23. The composition of claim 22, wherein the ligand has binding affinity for endothelial tumor cells for internalization by such cells.

10

24. The composition of claim 22, wherein the ligand is selected from the group consisting of E-selectin, Her-2 and FGF.

15

25. The composition of claim 22, wherein said ligand is selected from the group consisting of c-erbB-2 protein product of the HER2/neu oncogene, epidermal growth factor (EGF) receptor, basic fibroblast growth receptor (basic FGF) receptor, vascular endothelial growth factor receptor, E-selectin receptor, L-selectin receptor, P-selectin receptor, folate receptor, CD4 receptor, CD19 receptor,  $\alpha\beta$  integrin receptors, and chemokine receptors.

20

26. The composition of claim 1, wherein said liposomes further comprise a cationic lipid.